PRRX1 promotes malignant properties in human osteosarcoma

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Abstract

Paired related homeobox 1 (PRRX1) is a marker of limb bud mesenchymal cells, and deficiency of p53 or Rb in Prrx1-positive cells induces osteosarcoma in several mouse models. However, the regulatory roles of PRRX1 in human osteosarcoma have not been defined. In this study, we performed PRRX1 immunostaining on 35 human osteosarcoma specimens to assess the correlation between PRRX1 level and overall survival. In patients with osteosarcoma, the expression level of PRRX1 positively correlated with poor prognosis or the ratio of lung metastasis. Additionally, we found PRRX1 expression ~~on~~ in 143B cells, a human osteosarcoma line with a high metastatic capacity. Downregulation of PRRX1 not only suppressed proliferation and invasion but also increased the sensitivity to cisplatin and doxorubicin. When 143B cells were subcutaneously transplanted into nude mice, PRRX1 knockdown decreased tumor sizes and rates of lung metastasis. Interestingly, forskolin, a chemical compound identified by Connectivity Map analysis using RNA expression signatures during PRRX1 knockdown, decreased tumor proliferation and cell migration to the same degree as PRRX1 knockdown. These results demonstrate that PRRX1 promotes tumor malignancy in human osteosarcoma.

Keywords: PRRX1, osteosarcoma, tumor malignancy, invasion, drug resistance, Connectivity Map analysis

Abbreviations; Paired Related Homeobox 1 (PRRX1), Osteosarcoma (OS)